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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,841	07/27/2005	Robert Wieder	601-1-134PCTUS	1291

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EXAMINER	
NATARAJAN, MEERA	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
04/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,841	WIEDER, ROBERT	
	Examiner	Art Unit	
	MEERA NATARAJAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,9,12,53,54,60 and 61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 9, 12, 53, 54, 60 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments in the reply filed on 2/17/2009 is acknowledged and entered into the record.

2. Accordingly, Claims 1, 5, 9, 12, 53, 54, 60 and 61 are pending and will be examined on the merits.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.,* 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1, 5, 9, 12, 53, 54, 60 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varner et al. (US Patent #7311911) in view of Li et al. (US PgPub 20040048312).

6. The Claims are drawn to a method comprising administering to a mammal with breast caner as adjuvant therapy an agent effective in blocking the interaction of alpha 5

beta 1 with fibronectin. The method comprises disrupting survival signaling from a bone marrow microenvironment to single breast cancer cells or breast cancer cell micrometastases, inhibiting cellular proliferation or inducing cell death or cellular differentiation of single breast cancer cells or breast cancer cell micrometastases, and sensitizing to or potentiating chemotherapy or radiation therapy in mammals undergoing treatment for breast cancer.

7. Varner et al. teach a method comprising contacting alpha 5 beta 1 with an agent that interferes with specific binding of the alpha 5 beta 1 integrin to its ligand, fibronectin (see Abstract). Varner et al. disclose *in vivo* methods of administering said agent to an individual suffering from breast cancer (see Abstract and Claim 62). Varner et al. disclose the agent that interferes with the binding of alpha 5 beta 1 with fibronectin can be a peptide (see Claim 13), an integrin antibody (see Claim 15), a nonpeptide organic molecule (see Claim 16), or an agent linked to a chemotherapeutic drug (see Claim 20). Varner et al. teach the active steps of Claim 1 and 12 and therefore would inherently disrupt survival signaling, inhibit cell proliferation, induce cell death or differentiation, and sensitize the cells to chemotherapy or radiation therapy when said agent is administered to a human suffering from breast cancer. In addition, Varner et al. disclose that administration to a subject can either be over a relatively short period or time or can be over a more prolonged period of time. Varner et al. states one of skill in the art would know what treatment protocol to execute based on an individuals' factors including age, general health, route of administration, and number of treatments to

achieve the most effective therapy. Varner et al. does not specifically disclose an adjuvant therapy. This deficiency is made up for by Li et al.

8. Li et al. teach the use of an antibody which binds to an integrin to inhibit growth of a cancer cells. Li et al. disclose the anti-integrin antibody "can be employed as adjuvant therapy at the time of the surgical removal of a cancer expressing the antigen in order to delay the development of metastasis" (see paragraph [0136]).

9. It would have been prima facie obvious to one of ordinary in the art at the time the claimed invention was made to have administered the agent taught by Varner et al. as adjuvant therapy as taught by Li et al.. Based on the teachings of Varner et al that administration to a subject can either be over a relatively short period or time or can be over a more prolonged period of time and the teachings of Li et al. that anti-integrin antibodies which inhibit tumor growth can be used as adjuvant therapy, one of skill in the art would have been motivated with a reasonable expectation of success to administer the anti-alpha-5-beta-3 integrin antibody as adjuvant therapy to prevent metastasis.

Response to Arguments

10. Applicants argue the amended claims comprising a method of administering an agent effective in blocking the interaction of alpha 5 beta 1 with fibronectin as "*adjuvant*" therapy is novel over the prior art. Applicants argue "this amendment clarifies the timing of administration of the agent of the invention to an adjuvant setting and, in so doing, defines the patient population to be treated as breast cancer patients who have received previous treatment to eliminate detectable disease. Such patients have no

detectable disease, but are treated with adjuvant therapy to prevent relapse of disease". These arguments have been carefully considered but not found persuasive. Based on the teachings of Varner et al. that different therapeutic protocols can be used to achieve the most effective treatment regime, including the timing and number of treatments, one of ordinary skill in the art would have been motivated to perform the method taught by Varner et al. as adjuvant therapy to prevent re-occurrence of disease.

Conclusion

11. Claims 1, 5, 9, 12, 53, 54, 60 and 61 are rejected.

12. No Claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is (571)270-3058. The examiner can normally be reached on Monday-Thursday, 9:30AM-7:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643